the publications of His, Retzius, Cajal and Ranvier; the selection of the drawings and their execution deserve equally high praise.

The second part of the volume treats the anatomy of the fore-brain.

The first chapter (pp. 233-386) covers the general morphology, the convolutions and fissures, the base of the fore-brain, and the configuration of its interior. Numerous drawings from photographs take the place of the customary diagrams.

The second and the third chapters (pp. 387-666) are practically a description of macroscopic and microscopic serial sections through the cerebrum, made in different directions, and forming the most complete atlas of those parts published so far.

A chapter on the cerebral cortex (pp. 667-741) and one on the white substance of the cerebral hemispheres (pp. 742-810) form the end of this first volume, rich in pathological observations with regard to the association systems.

The second volume will bring the description of the remaining parts and a systematic analysis of the fibre tracts.

The style is very clear, the current epitome on the margin of the pages very convenient. Schematic drawings are avoided; the figures are very accurately drawn, and clear.

Thus we have before us the first half of a work of fundamental importance for the progress of neurology, destined to bring the clinician into closer touch with the anatomical literature that is scattered in monographs and journals, and is here, for the first time, made satisfactorily accessible. Meritorious as the smaller works of Edinger, Obersteiner, Féré, Debierre, and the purely anatomical treatises are, none of them could give such a full account of the minute details that interest the clinicians and pathologists of to-day.

It is to be hoped that the second volume will soon follow and bring a very accurate index. ADOLF MEYER.

URIC ACID AS A FACTOR IN THE CAUSATION OF DISEASE: A CONTRIBUTION TO THE PATHOLOGY OF HIGH ARTERIAL TENSION, HEADACHE, EPILEPSY, MENTAL DEPRESSION, GOUT, RHEUMATISM, DIABETES, BRIGHT'S DISEASE AND OTHER DISORDERS. By Alexander Haig, M.A., M.D., Oxon., F.R.C.P. Second edition, with 36 illustrations. London: J. and A. Churchill, 1894.

The appearance of a second edition of Dr. Haig's volume on uric acid in relation to disease is not only one of the many indications of a growing interest in the disorders of metabolism and general nutrition, but is also strong evidence that people prefer a bad book on an interesting subject to no book at all. For it must be said that the book before us represents a most unscientific attempt to fix the pathology of uric acid excretion and to refer a formidable array of diseases to the presence of an excess of uric acid in the blood or tissues. That this is a mild criticism of Dr. Haig's undertaking is shown in even a cursory review of its leading features.

In the first chapters of his book the author gives his views on the production and elimination of uric acid. Briefly stated these views are as follows:

First, the ratio of formation of uric acid to urea in the body is constant.

Second, since this ratio is constant, any deficiency in the amount of uric acid excreted by the urine must mean that there is a corresponding retention of uric acid in some part of the body.

Third, the urea produced in the body is never retained in excess, but is execreted promptly as it is formed ; therefore, as the ratio of uric acid to urea in the urine is clearly a variable one, the quantity of uric acid in the body must constantly vary.

Fourth, any excess of uric acid in the body may be in the tissues or in the blood. If in the tissues, the uric acid may either (*a*) lie latent, as in the spleen, without causing symptoms, or (*b*) give rise to symptoms, such as the symptoms of gout, when the deposit is in the joints. If in the blood, the dissolved uric acid causes the most striking symptoms and is responsible for the numerous diseases whose description makes up by far the greater part of Dr. Haig's volume.

Fifth, the proportion of uric acid in the blood or tissues at a given time depends on the reaction of the blood ; a reduction of the alkalinity of the blood causes a precipitation of uric acid in the tissues, an increase in alkalinity leads to the solution by the blood of the uric acid in the tissues, and favors the eventual elimination of the uric acid. Food, exercise, fatigue, perspiration, alkalies, acids, quinine, lead, mercury and a host of drugs owe their influence upon the organism to their effect in modifying the alkalinity of the blood.

Although these views have been more or less skillfully elaborated by the author, they form the basis, as stated above, of his conception of the pathology of uric acid excretion. Let us consider some of these fundamental propositions.

The statement that the ratio of uric acid and urea formation in the body is a constant one is without any foundation, and entirely ignores the extreme complexity of the chemistry of organic life, and the variations in circulating proteids, which render such an assumption in the highest degree improbable on *à priori* grounds. The burden of proof certainly rests in this instance on him who ventures on an assumption so removed from probability. The fact that in health the ratio of uric acid to urea *excreted* daily varies but little is of course no evidence whatever that the ratio of *formation* of those substances remains the same in all conditions of health and disease. The idea that the urea produced in the body is never retained in excess, but is promptly excreted, was disproved by the classical researches of Bright, Christison and Rayer in England early in this century, and the reviewer has definite proof from personal research that an excess of urea in the blood, amounting to 100 or 200 per cent., is no uncommon occurrence in nephritis, even when there are no symptoms of uremia. The recent careful work of Roberts affords no evidence that the precipitation of uric acid in the form of tophi of gout is due to an excess of acids in the blood, and furnishes strong reason for thinking that it is an excess of salines that is the leading factor in the precipitation of the urates. There is no foundation for Haig's statement that the administration of acids rids the blood of its uric acid by precipitating it into the tissues, and conversely, that the use of alkalies causes this precipitate to redissolve To substantiate this statement, it would be necessary to make an elaborate series of experimental observations by means of the most perfected technical methods—an undertaking beset by great practical difficulties—and of such observations none are brought forward.

An excess of uric acid in the blood is the cause, according to Haig, of an increase of arterial tension, due to contraction of peripheral blood vessels. There is, however, no experimental evidence to show that uric acid dissolved in the blood has any such effect, while we have satisfactory evidence, especially that derived from the experimental work of Roy and Sherringham, that the chief chemical cause of contraction of the arterioles of the brain is increased alkalinity of the blood, while the injection of acids into the circulation causes a relaxation of the vascular coats. Haig has by no means ruled out the influence of varying alkalinity of the blood in modifying arterial pressure. Even the proposition that the uric acid content of the blood increases with the blood alkalinity is far from being established.

The twelve chapters following those to which reference has been made are occupied with the application of Haig's physiological principles to the explanation of pathological processes. The variety of the processes that are attributed to the action of uric acid is shown by the titles of some of the chapters:

Headache; Epilepsy, Convulsions and Hysteria; Mental Depression and Fatigue; Asthma and Bronchitis; Dyspepsia and Gout of the Intestines; Raynaud's Disease; Paroxyismal Hæmoglobinuria and Anæmia; Albuminuria and Bright's Disease; Glycosuria and Diabetes Mellitus; Gout; Rheumatism and Morbus Cordis.

It would be useless, even if it were possible, to follow Haig's elaborate but incoherent argumentation for the causation by uric acid of the various diseases already referred to. It would also be quite useless to refute one after another his various "facts" and statements of opinion (some of which sound reasonable enough, but the majority of which are evidently mere speculation), for some of the most absurd views, born of the fancies of the moment, might require years of research to directly and scientifically controvert.

We have, however, another method, more radical and less difficult, of estimating Haig's claim for uric acid as a factor in disease This consists simply in inquiring into the nature of the direct evidence that uric acid causes disease.

If uric acid in the blood, uricacidamia, is the cause of migraine, epilepsy, anæmia, hæmoglobinuria, albuminuria, chronic nephritis, rheumatism, etc., we should expect to find in the blood in these states an excess of uric acid.

The finding of such an excess would not, of course, necessarily mean that this excess stands in the relation of a cause to these diseases, for some other interpretation of the excess might be the correct one, but the point we wish to insist on here is that the demonstration of this excess in the blood is essential as a foundation on which to build an intelligent hypothesis of the uric acid causation of disease. The observations on the uric acid of the urine will not answer; they may be highly suggestive and doubtless are, but they do not give us positive evidence of the conditions of the blood as regards uric acid. Again, we have already seen that Haig's cast-iron uric acid ratio theory is without any scientific foundation, and hence all the conclusions based on it are void.

What evidence, then, is offered us regarding the blood? The uric acid of the blood was estimated (pp. 46-52) in a case of cerebral hæmorrhage, in one of cellulitis, in one of hæmoptysis, in eleven cases with urate deposits in the joints, in eleven cases without urate deposits in the joints, in some cases of pneumonia, in a case of pneumonia with delirium tremens, in a case of morbus cordis, and in dogs and monkeys.

The figures obtained varied a good deal, and are too scattered to offer a basis (even supposing the figures to be correct) on which to generalize as to the influence of disease on the uric acid content of the blood. There are no observations on the blood in epilepsy, or headache, or nephritis, or on the greater number of diseases which the author refers to uric acid. Yet these results are garnished with suppositions in such a way as to make them prove almost everything the writer wishes. But this is not all. The technical means by which Haig reaches his results are open to the severest criticism.

In studying uric acid he employs the Haycraft method. This in the case of urine is admissable, for although the results given by it are high, the error is probably reasonably constant. In the case of the blood, however, the error which may be introduced is enormous. For the Haycraft method is one in which the uric acid is estimated by the silver precipitate which not only includes what uric acid is present, but also other extractives which are present in the blood in relatively large and varying amounts. This method is, therefore, wholly unsuited to the use to which Haig, without any apparent appreciation of its character, has put it, and its results must be regarded as nothing short of worthless. But it is only right to mention the fact that Haycraft designed his method for the urine and not for the blood. It may be objected that it is a severe test to require the demonstration of the actual presence of an excess of uric acid in the blood as proof that such excess is related to disease in the manner claimed. It is a severe test, but nothing short of such an demonstration would constitute a basis for the views of Haig. Clever argumentation cannot take its place.

There is no evidence in the volume under consideration that the author has ever seriously considered the possibility that the presence of uric acid in the blood can be regarded as standing in any other relationship to disease than a causative one. It is the opinion of the reviewer, based on extended personal observation, that the excess of uric acid in the urine which is met with in disease is to be regarded as the result and expression of general nutritive disturbance or digestive disorder, and not as the cause of disease, except in a limited way.

It would be out of place to enter into this question here, but it should be noted that the clinical evidence, which points strongly to the correctness of this view, is reinforced by the studies of Horbaczewski as to the origin of uric acid and allied bodies. Horbaczewski's careful experimental observations indicate that uric acid is derived largely from the nuclein in the nuclei of the body-cells, especially the white blood-cells, and in consequence of their continual breaking down, and it is certain that uric acid, with its allied leucomaines, xanthine and hypoxanthine, guanine and adenine, can be obtained by the destructive transformation of nuclein. We cannot but consider it singular that this important work of Horbaczewski's, with all that it suggests, should have been not even mentioned in a volume dated 1894 dealing with the subject of uric acid.

The subject of uric acid in connection with disease is one where study is beset with difficulties, and it would be asking too much of any writer to make a wholly satisfactory book on it in the present state of our knowledge. We do not criticise Haig's book because it fails to settle the relation of uric acid to disease, but chiefly because of its pernicious method, the faulty observations it records, and the loose generalizations it puts forward. Such a book cannot fail to do harm by disseminating false yet plausible ideas, which few practitioners have time to investigate and to controvert for themselves. On the other hand, the book has probably done good by stimulating inquiry and discussion in a field of medicine which is most important from a practical as well as from a theoretical standpoint.

In conclusion, it may be pointed out that we must not take too narrow a view of the subject under consideration. An understanding of the rôle which uric acid plays in animal nature is intimately bound up with the more general problems of nutrition, with the subjects of digestion, absorption, the formation and destruction of the blood, and the metabolic processes generally. No progress can be made in our understanding of uric acid and its allied leucomaines without corresponding progress along these collateral and overlapping lines

We believe the day will come, though it be distant, when some patient investigator, of the type of Darwin, with a vast array of facts before him, will study these facts in their relations to one another, and enable us to see order and obedience to the larger laws of pathology, where at present there is little but the confusion of seemingly unrelated facts.

C. A HERTER.

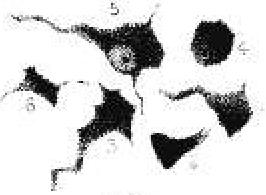

Fig. 1

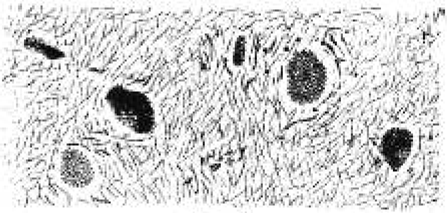

Fig. 2.

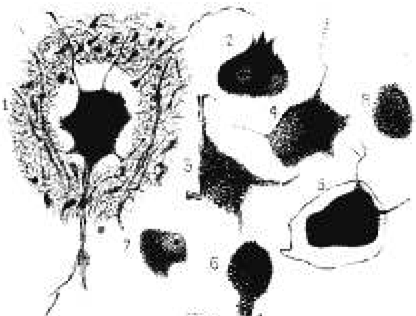

Fig. 4

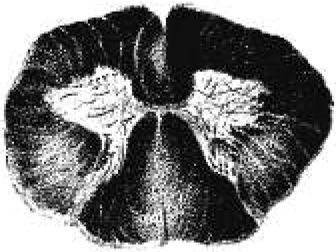

Fig. 3

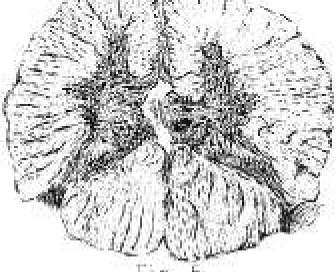

Fig. 5

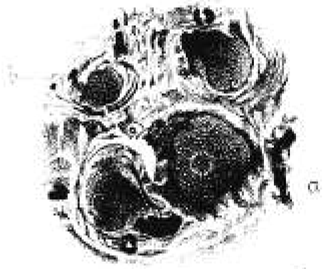

Fig. 6

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